

DOCKET NO.: ISPH-0589

PATENT

## REMARKS/ARGUMENTS

After entry of this paper, claims 25-35 are pending. Claims 4-10, 12, 13, 15 and 24 are canceled in an effort to place the application in condition for allowance. Applicants reserve the right to prosecute these claims in a timely filed continuation application.

For ease of review, Applicants added new claims 25-35 instead of amending the previously pending claims (which are canceled in this paper). New claims 25 and 35 recite additional embodiments of the invention, which subject matter clearly falls under the subject matter of previously pending and now canceled claim 4. Claims 26-34 are newly added, parallel canceled claims 4-9, 12-13, and 15, and depend directly or indirectly from new claim 25.

Specifically, new claims 25 and 35 are drawn to antisense oligonucleotides 20 to 50 nucleobases in length, which oligonucleotides are clearly encompassed by the antisense oligonucleotides 8 to 50 nucleobases in length recited in canceled claim 4 and previously searched by the Examiner. The antisense oligonucleotides of new claims 25 and 35 must also contain the sequence of SEQ ID NO: 28 which specifically hybridizes with nucleotides 981-1000 of SEQ ID NO: 3. As the Examiner is aware, SEQ ID NO:28 hybridizes with a specific section of SEQ ID NO: 3 and this section is encompassed by the 14-1741 range specified in canceled claim 4, which was previously searched by the Examiner. These newly added claims are not broader in scope than canceled claim 4, and, in fact, describe a narrower embodiment of the previously claimed invention. Therefore, the subject matter of the newly added claims

DOCKET NO.: ISPH-0589

PATENT

falls under any subject matter searched by the Examiner to date.

The newly added claims are supported in the originally filed specification and claims and specifically in Table 1 on page 89. No new matter is added by these new claims.

**Information Disclosure Statement**

*The Examiner indicated that the IDS filed on December 27, 2004 was not considered since the same was not scanned into the Image File Wrapper system and was unavailable for review.*

*The Examiner indicated that consideration of the IDS dated December 27, 2004 will be addressed in the next Office Action.*

Applicants respectfully request that a non-final Office Action be issued if the Examiner rejects the pending claims over documents that were cited in the IDS filed on December 27, 2004.

**35 USC § 103(a) Rejection**

*Claims 4-10, 12, 13, 15, and 24 are rejected under 35 USC § 103(a) over Chang et al. (US Patent No. 5,968,749 - Chang I) or Chang et al. (US Patent No. 5,484,727 - Chang II) in view of Baracchini et al. (US Patent No. 5,801,154) and Taylor et al. (Drug Disc. Today, 1999, 4(12):562-567 for the same reasons as set forth in the Office Action dated July 16, 2003.*

Applicants respectfully request reconsideration and withdrawal of this rejection as applied to new claims 25-35 for the following reasons.

With respect, Applicants respectfully disagree with the Examiner that each reference was argued individually in

DOCKET NO.: ISPH-0589

PATENT

the Response filed by Applicants on October 14, 2004. As support, Applicants direct the Examiner's attention to the paragraphs in Applicants' filed Response on page 8, lines 14-17; page 9, lines 3-14; and page 9, lines 22-28 where Applicants in fact discussed how all of the cited references in combination do not teach or suggest the present invention. Further, Applicants maintain that the discussion of each document individually was necessary to provide the relevance of the same to the combination of the references together. For example, the cited references must be analyzed individually prior to analyzing the combination of the same with other cited references to determine if the references are analogous, or if one or more of the references teach any from the claimed invention or the other reference(s), among others.

In view thereof and as noted above, Applicants' presently claimed invention is drawn to an antisense oligonucleotide that is 20 to 50 nucleobases in length and targeted to a nucleic acid molecule encoding acyl coenzyme A cholesterol acyltransferase-1 (ACAT-1) (SEQ ID NO: 3). The oligonucleotides of the presently pending claims must contain the sequence of SEQ ID NO: 28. The antisense oligonucleotides of the invention also specifically hybridize with at least an 8 nucleobase portion of the nucleic acid molecule encoding ACAT-1 and inhibit expression of the nucleic acid molecule encoding ACAT-1.

With respect, Applicants maintain that the combination of Chang I and/or II, Baracchini and Taylor does not make a *prima facie* obviousness rejection of the pending claims. Specifically, none of Chang I, Chang II, Baracchini, or

DOCKET NO.: ISPH-0589

PATENT

Taylor refer to oligonucleotides that must contain the nucleic acid sequence of SEQ ID NO: 28. In fact, the Examiner noted that "Chang was not relied upon for a teaching of specific antisense sequences"<sup>1</sup> and that "...both Baracchini and Taylor are considered to provide information sufficient to make, test, and use antisense oligos..."<sup>2</sup>. It was Applicants who first suggested the desirability of using this sequence in the oligonucleotides of the present invention. None of the cited references in combination point to oligonucleotides that must contain the sequence of SEQ ID NO: 28, i.e., a sequence that specifically hybridizes to nucleotides 981-1000 of SEQ ID NO: 3.

Therefore, since no combination of the cited references teaches or suggests oligonucleotides that must contain the sequence of SEQ ID NO: 28, no combination of these references teaches or suggests the use of the same in inhibiting expression of the nucleic acid molecule encoding ACAT-1.

Therefore, no combination of Chang I, Chang II, Baracchini, or Taylor teaches or suggests the present invention. Reconsideration of this rejection is requested.

<sup>1</sup> Page 5, line 17 of January 13, 2005 Office Action

<sup>2</sup> Page 5, line 22 through page 6, line 1 of the January 13, 2005 Office Action

DOCKET NO.: ISPH-0589

PATENT

The Director is hereby authorized to charge any deficiency in any fees due with the filing of this paper or during the pendency of this application, or credit any overpayment in any fees to our Deposit Account Number 08-3040.

Respectfully submitted,

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